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EXAMINER

WILDER, CYNTHIA B

ART UNIT PAPER NUMBER

1637

DATE MAILED: 08/07/2002

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/053,611

Applicant(s)

POLYAK ET AL.

Examiner

Cynthia Wilder

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 and 29-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 and 29-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

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DETAILED ACTION

1. Applicant's preliminary amendment filed in Paper No. 5 is acknowledged and has been entered. Claims 17-28 have been canceled. Claims 1, 2, 9-11, 30 and 31 have been amended. Claims 1-16, 29-32 is pending. An action on the merit appears below.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 1, 9, 10, 29, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by ~~the~~ Alonso et al. (Electrophoresis, May 1997). Regarding claims 1 and 32, Alonso et al. teach a method to aid in detecting the presence of tumor cells in a patient wherein the sample is a tumor, comprising the steps of determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a tumor of the patient but not in normal tissue of the patient, and identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient (page 682, "Abstract" and section 2.1).

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Regarding claim 9, Alonso et al. teach wherein the step of determining comprises amplifying mitochondrial DNA (page 682, col. 2, section 2.1, lines 28-36).

Regarding claim 10, Alonso et al. teach wherein the step of determining comprises sequencing mitochondrial DNA (page 683, col. 1, section 2.4, lines 26-36).

Regarding claim 29, Alonso et al. teach wherein the mutation was identified previously in a tumor of a patient (page 682, col. 1, lines 23-25 and col. 2, lines 6-8).

Regarding claim 31, Alonso et al. teach wherein the method comprise the step of testing a normal tissue of a patient to determine the absence of mutation (page 683, section 3.1, lines 39-45 bridging col. 2, lines 1-4). Therefore, the claimed invention of claims 1-3, 9, 10, 12-16, 29 and 31 are anticipated by the reference of Alonso et al.

Claim Rejections - 35 USC § 102/103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 2, 3 and 12-16 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Alonso et al as applied to claims 1, 9, 20, 29 and 31 above. Claim 2 is drawn to an embodiment of claim 1, wherein, prior to the step of determining, the mutation has been identified in a tumor. Alonso et al. teach wherein prior to the step of determining, an increase frequency of heteroplasmic mutations are identified in mitochondrial DNA.

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Alonso et al further identifies a deletion mutation in a gastric tumor (page 682, col. 2, lines 4-8).

The preceding rejection is based on the judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because the reference is silent with regard to “the mutation being a single basepair mutation”.

However, the “single basepair mutation” is deemed to be inherent in the recitation of “heteroplasmic mutations of mitochondrial DNA” because “heteroplasmic mutations” are interpreted as encompassing both single basepair mutations and/or multiple base alterations in a sample. Additionally, the reference teaches wherein a heteroplasmic mutation of the mitochondrial DNA comprise a single nucleotide change (page 684, col. 2, lines 6 and 7). Therefore, the burden is on Applicant to show that the claimed “mutation identified in a tumor prior to the step of determining” is different or non-obvious over that of Alonso et al.

Regarding claim 3, Alonso et al. teach wherein the cell sample is from a tissue sample of a cancerous tumor (page 682, lines 1-4 of Abstract and col. 2, lines 28-30).

Regarding claims 12-16, Alonso et al. teach wherein the single basepair mutations are insertion, deletion, transition and/or homoplasmic mutation (page 683, Table 1 and 685, col. 1, lines 1-8, especially line 4). Alonso et al. also disclose wherein the mutation is a substitution mutation (page 682, col. 1, lines 19-21).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

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matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 4-8 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alonso et al. in view of Sidransky (5,935,787 effective filing date August 1994) and Sidransky (6,025,127, filing date January 1994). Regarding claims 4-8, Alonso et al. teach a method to aid in detecting the presence of tumor cells in a patient, comprising a number of method steps wherein a patient is identified as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient. The method of Alonso et al differs from that of the claimed invention in that Alonso et al. does not expressly teach wherein the cell sample is from blood, urine, sputum, saliva, or feces. However, it is known in the art that tumor cells are shed in the bloodstream and other bodily fluids. For example, Sidransky teaches a method of detecting primary tumors and metastatic sites in a patient, wherein a cell sample is from blood, urine, sputum, stool or any bodily fluids that drains a body cavity (col. 4, lines 26-29). It would have been obvious to one of ordinary skill in the art at the time the invention was made to obtain the claimed invention because the skilled artisan would have been motivated to provide cell sample from a

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variety of sources for the convenience of diagnostic testing to the practitioner and patient. Additionally, the source of the cell sample would have been determined by one of skill in the art based on availability of starting material, desired results and patient consent.

Regarding claim 30, the Examiner takes notice that chemotherapy and radiation along with drug therapy are routinely used in the art as an anti-cancer therapy to patients having malignant tumors. Additionally, the progress of the anti-cancer therapy to the patient is routinely monitored to determine the effectiveness of the treatment in reducing or eradicating tumor cell growth, for example as taught by Sidransky (6,025,127). Sidransky teaches monitoring the progress of a patient having a malignant tumor using chemotherapy as an anti-cancer therapy (col.2, lines 65-67).

8. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Alonso et al. and further in view of Chee et al. (Science, October 1996). Regarding claim 11, Alonso et al. teach a method to aid in detecting the presence of tumor cells in a patient comprising the steps of determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient and identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient. The method of Alonso et al. differs from that of the claimed invention in that Alonso et al. do not teach wherein the step of determining comprises hybridization of DNA amplified from the mitochondrial genome of the cell sample to an array of oligonucleotides which comprises matched and mismatched sequences to human mitochondrial genomic DNA. In a method for determining mutation in mitochondrial genome, Chee et al. teach wherein the steps comprises hybridization of DNA from the mitochondrial genome to an array of oligonucleotides which comprise matched and mismatched sequences to

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human mitochondrial genomic DNA (page 611, col. 2, lines 5-26 and col. 3, lines 1-22). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to obtain the claimed invention because the skilled artisan would have been motivated determine single basepair mutation using hybridization to a DNA array with a reasonable expectation of success by the advantages taught of Chee et al. that hybridization to a high density DNA array allows sequence alterations in the human mitochondrial genome, to be detected with single-base resolution and unprecedented efficiency (Abstract). The authors further add that the method can be used to characterize the spectrum of sequence variation in a population and can be applied to the analysis of many genes in parallel (page 613, col. 1, lines 2-6). Chee et al. also teach that the sequence of a gene, its spectrum of change in the population, its chromosome location, and its dynamic of expression can be determined using the method of hybridization with high density probe arrays (page 613, col. 1, lines 25-27 bridging col. 2, lines 1-3).

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ

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761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-16 and 29-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No.6,344,322 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '322 patent only slightly differs from the claimed invention in scope. For example, in the '322 patent the method to aid in detecting the presence of tumor cells in a patient comprises steps of identifying 12 specific single basepair mutations in a mitochondrial genome of a cell sample of a patient whereas the claims of the instant invention are not limited to any specific basepair mutations of the mitochondrial genome of a cell sample. The claims of the instant invention encompasses any single basepair mutations including those cited in the claims of the '322 patent. Thus, the difference in scope do not represent a patentable distinction.

Conclusion

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11. No claims are allowed.


12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 7:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group's Patent Analyst, Monica Graves at (703) 305-3002 or Group's receptionist at (703) 308-0196.

Cynthia B. Wilder, Ph.D.

July 31, 2002


KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

8/1/02